DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214) 253-5200 Fax:(214) 253-5314 Industry Information: www.fda.gov/oc/industry	03/18/2013 - 04/16/2013* FEI NUMBER 3000203232

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Mr. Raymond J. Bertrand, President and Pharmacist in Charge

FIRM NAME	STREET ADDRESS
Apothecure, Inc	4001 Mcewen Rd Ste 100
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Dallas, TX 75244-5021	Producer of Sterile Drug Products

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

There is a failure to thoroughly review the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically,

A) SOP #9.040 entitled, "Sterility Testing of a Finished Preparation" (Effective date: 6/12) documents that an investigation should be conducted in the event that contamination is observed.

Your firm's investigations into sterility (Plate Contamination or (b) (4)) or endotoxin failures were incomplete or absent for at least 28 lots of injectable drug products for the period between 3/2012 and 3/2013.

A total of three lots with (b) (4) inconclusive testing results were released to distribution without further investigation. All remaining lots which failed testing for sterility or endotoxin were destroyed.

Each failed or inconclusive (b) (4)) result is identified in the following table:

Product	Lot #	Plate Contamination Test Result Date/#CFU's	Endotoxin Failure Date/#EU/ml	(b) (4) Failure Date/Result	Investigation
Hydroxocobolamin 1mg/ml	20130219@1	3/12/13; CFU's:36	ND*	N/A	Y
HCG 5,000 Units	20130211@3	3/4/13; 0 CFU	ND*	2/21/13; 114/-E/M (Inconclusive)	N
Curcumin 5mg/ml	20130109@2	1/23/13; CFU's: TMTC**	ND*	N/A	N

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Stephen D. Brown, Investigator
H.L. Jamillah Selby, Investigator
John T. Chapman, Regional Emergency Response Coordinator

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Sodium Hyaluronate 35mg/ml	20121212@8	1/7/13; 0 CFU	1/7/13(40.9/EU/ml)	N/A	Y
Hydroxocobolamin/Lidocaine 1mg/ml	20121226@11	1/4/13; CFU's: 1	ND*	N/A	N
Thioctic Acid 200mg/ml	20121029@19	11/21/12; 0 CFU	11/19/12(55EU/ml)	N/A	Y
Hyaluronic Acid 20mg	20121101@19	11/15/12; 0 CFU	11/16/12(58EU/ml)	N/A	Y
L-Carnitine 500mg/ml	20121106@14	11/19/12; CFU's:1	ND*	N/A	Y
Sodium Hyaluronate 25mg/ml	20121102@12	11/15/12; 0 CFU	11/16/12 (195EU/ml)	N/A	Y
Sodium Citrate 4%	20121030@36	11/12/12; CFU's:1	ND*	N/A	Y
Hyaluronidase 150u/ml	20121026@31	11/9/12 146 CFU's	ND*	N/A	N
EDTA Calcium	20121008@22	10/23/12; 0 CFU	11/1/12(758EU/ml)	N/A	Y
Collagenase 1000u/ml	20121025@21	11/8/2012 CFU's:129	ND*	N/A	Y
Hydroxocobalamin 1mg/ml	20121010@6	10/23/12 TMTC**	ND*	N/A	Y
Vitamin C 500mg/ml	20121019@7	10/31/12; CFU's:1	ND*	N/A	Y
Prolotherapy #1 10ml	20121019@26	11/1/12; CFU's:1	ND*	N/A	Y
L-Theanine 30ml 100mg/ml	20121019@30	11/1/12; CFU's:1	ND*	N/A	Y
HCG 5000 units	20121008@6	ND*	ND*	10/18/12; 470/-E/M (Inconclusive)	N
Deoxycholic Acid 50mg/ml	20121002@16	10/15/12; CFU's:1	ND*	N/A	Y
Strontium Chloride 1mg/ml	20120911@8	9/26/12; CFU's:84	9/21/12; .36EU/ml	N/A	Y
Methylcobalamin 1mg/ml	20120904@10	9/20/12; 0 CFU	ND*	9/10/12; 9/4E/M	N
Taurine 50mg/ml	20120821@72	9/5/12; CFU's: 339	ND*	N/A	N
Laureth-9	20120723@7	8/3/12; CFU's:14	ND*	N/A	N
Grape Seed Extract	20120711@4	7/27/12; 0 CFU	7/24/12; 13300 EU/ml	N/A	N
Sodium Bicarbonate 8.4%	20120716@7	ND*	ND*	7/20/12; 3/1E/M	N
Grape Seed Extract 10ml 15mg/ml for Injection	20120620@4	7/12/12; 0 CFU	7/10/12; 22200EU/ml	N/A	N
Selenium 40mcg/ml	20120430@28	5/9/12; CFU's:4	ND*	N/A	N
Sermorelin/GHRP-6	20120423@61	5/15/12; 0CFU	ND*	5/4/12; 195/-E/M (Inconclusive)	N

* Not Determined

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** Too Many to Count

Some examples where an investigation was absent include the following:

1. Methylcobalamin Buffered, 30ml, 1mg/ml for Injection, lot #20120904@10 (Production date: 9/4/12 Beyond Use Date: 8/1/13)

Your contract laboratory utilized a (b) (4) microbial detection test which determined that lot #20120904@10 failed sterility (Result: 9/4E/M). Subsequent Plate Contamination (b) (4) test) testing revealed that the lot met specifications. There was no investigation into the failed (b) (4) test.

Lot #20120904@10 was released for distribution.

2. Curcumin, 5mg/ml, lot #20130109@2 (Production date: 1/9/2013 Beyond Use Date: 12/31/13)

Lot #20130109@2 failed a Plate Contamination test with a result of "TMTC" (Too many to count) . An investigation was not performed.

3. Hydroxocobalamin, 1mg/ml, lot #20121226@11 (Production date: 12/26/12 Beyond Use Date: 4/30/13)

Lot #20121226@11 failed a Plate Contamination test with a result of "TMTC" (Too many to count). An investigation was not performed.

An example of an investigation which was incomplete consists of the following:

1. Hydroxocobalamin 1mg/ml, lot #20130219@1 (Production date: 2/19/2013 Beyond Use Date: 9/1/2013)

Lot #20130219@1 failed a Plate Contamination test with a result of 36 CFU's.

Your firm issued a "Remedial Action Form" (undated) which indicated that improper aseptic technique had been observed by a pharmacist. Re-training of the technician was recommended.

In addition, your firm issued an "Identification Form" dated 3/14/13 which documented the following:

- Lot #20130219@1 failed "sterility"
- Production logs were reviewed
- Possible errors with aseptic technique
- Your firm made a recommendation to obtain a (b) integrity tester. However, this recommendation was not

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implemented.

The investigation was incomplete in that various parameters to include the following were not evaluated:

- Speciation of contaminating organism
- Sterile (b) (4)
- Room pressurization
- Laminar flow operation
- Assessment of container closure
- Sanitization procedures (Room, equipment, product containers, etc.)
- Evaluation of associated lots

No root cause was identified.

B) SOP #8.011.2 entitled, "Potency Testing" (Effective date: 6/27/12) documents, in part, that an investigation will be performed in the event that a product fails potency. Review of testing records for sterile, injectable drug products for the period between 3/12 and 3/13 revealed that at least 45 lots failed testing for potency. No investigations were conducted for any of the failed lots. Some examples consist of the following:

- Chromium 200mcg, lot #20120716@29 (Production date: 7/16/12, Beyond Use Date: 7/6/14)

Lot #20120716@29 failed with a potency result of 116%.

- DMPS 5ml, 50mg/ml, for Injection, lot #20120109@20 (Production date: 1/9/12 Beyond Use Date: 1/8/2013)

Lot #20120109@20 failed with a potency result of 123%.

- Dexpanthenol, 30ml, 250mg/ml for Injection, lot #20120106@46 (Production date: 1/6/2012, Beyond Use Date: 15/2013)

Lot #20120106@46 failed with a potency result of 85.2%.

All failed lots were destroyed.

C) SOP #9.030 entitled, "Particulate Testing for Sterile Preparations" (Date: 1/2013) provides guidance for the evaluation of vials of sterile, injectable drug products for particulates. Between 1/2013 and 3/2013, your firm identified at least 110 lots containing fibers and/or particulates for which

investigations were not conducted.

In each case, your firm conducted a 100% inspection by holding each amber vial below a light source against a white/black background. Vials identified as containing fibers and/or particulates were then removed and discarded. However, this method has not been validated.

The remaining vials from each lot were then distributed to consignees. Some examples consist of the following:

- Curcumin 10ml, 5mg/ml for Injection , lot #20130124@2 (Production date: 1/24/2013 Beyond Use Date: 12/31/13)

    1. Number vials produced: (b)
    2. Number vials removed: 2 (Testing), 3 (Particles), 4 (Unknown reasons), 4 (Unaccounted for)
    3. Number vials released: (b

- Folic Acid, 30ml, 10mg/ml for Injection, lot #20130215@13 (Production date: 2/15/2013 Beyond Use Date: 10/14)

    1. Number vials produced: (b)
    2. Number vials removed: 2 (Testing), 16 (Fibers)
    3. Number vials released (b)

- Vanadium, 10m1, 200mcg/ml for Injection, lot #20130206@6 (Production date: 2/6/2013, Beyond Use Date: 8/5/2013)

    1. Number vials produced: (b)
    2. Number vials removed: 2 (Testing), 18 (Fibers)
    3. Number vials released (b)

- Folic Acid, 5ml, 10mg/ml for Injection, lot #20130227@6 (Production date: 2/27/2013 Beyond Use Date: 11/1/14)

    1. Number vials produced: (b
    2. Number vials removed: 2 (Testing), 12 (Fibers)
    3. Number vials released (b)

D. Environmental Monitoring

SOP #5.005 entitled, "Environmental Testing for Laminar Flow Hood- EnviroTest" (Date: 6/12) describes the procedures for the testing (surface and air) of laminar flow hoods for bacteria, yeasts, and fungi. The testing is conducted monthly using a media paddle.

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Review of media paddle testing records revealed that the following tests conducted under static conditions failed:

- 11/29/12: Floor test (4 CFU)
- 10/15/12: Hood 1 (1 CFU)

There was no investigation.

OBSERVATION 2

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established, written, and followed.

Specifically, your firm did not establish written procedures to prevent microbiological contamination of drug products purporting to be sterile to include procedures for validation of aseptic processing. For example,

A)

1. SOP #7.007.3 entitled, "Media Fill for High Risk Compounding " (Date: 4/11) documents, in part, that a total of [redacted] will be used to conduct media fills.

Your firm conducted a media fill on 4/4/2011 which failed the Plate Contamination test for two different vials. There was no investigation. On 4/20/11, a subsequent media fill passed specifications. However, the media fill was deficient in that:

- The speciation of the contaminating organism (s) was not determined.
- The media fill failed to simulate a lot with the maximum number of vials (i.e. 300 vials)
- [redacted] integrity testing was not performed (i.e. multiple use of [redacted] observed on 3/18/13)
- The number and type of interventions was not included.
- The aseptic assembly of equipment (e.g., at start-up, during processing) was not included.

2. Your firm failed to validate the [redacted] used for the sterilization of injectable drug products. Some examples of [redacted] utilized by your firm consist of the following:

- [redacted]

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- (b) (4)
- (b) (4)
- (b) (4)
- (b) (4)

No integrity testing was performed on (b) (4) post (b) (4) .

In addition, your firm used a non-sterile (b) (4) which is not labeled as sterile or pyrogen free to (b) (4) the product, Curcumin 10ml 5mg/ml for Injection , lot #20130124@2 (Production date: 1/24/13 Beyond Use Date: 12/31/13) before using a (b) (4) to perform a final (b) (4) However, you have provided no data to demonstrate that the (b) (4) is non-shedding.

3. Your firm failed to validate (b) (4) used to sterilize injectable drug products and drug product components such as vials and stoppers. For example, you do not have temperature distribution studies or heat penetration studies utilizing current loading patterns for (b) (4) are used to sterilize injectable drug products using a "Liquid" cycle which utilizes a (b) (4) To date, the cycle has not been validated. Injectable drug products which are (b) (4) sterilized include:

- Vitamin A for Injection 10ml 50,000 IU/ml
- Vitamin D-2, 5ml, 125,000U/ml for Injection
- Vitamin D3, 5ml, Preserved, 50,000IU/ml for Injection
- Curcumin ,10ml, 5mg/ml for Injection

4. Smoke studies in the ISO 5 hoods were not conducted under dynamic conditions.

B. On 3/18/13, we observed the sterile (b) (4) of the drug product, L-Carnitine 30 ml 500mg/ml for Inejction (lot #20130307@5). The technician used non-sterile gloves, mask, gown and (b) (4) in the ISO 5 work area.

We noted that a technician first sterile (b) (4) the product into a flask in one ISO 5 hood (Hood #1) using (b) sterile (b) due to problems with clogging. After (b) (4) the technician did not integrity test any of the (b) . The technician then transferred the flask containing sterile (b) (4) product, uncovered, to another adjoining ISO 5 hood (Hood #2) through the ISO 7 area.

The same technician was observed filling the product into vials and picking up and placing stoppers on the tops of the vials with non-sterile gloved hands.

Lot #20130307@5 was later discarded by your firm after we informed managment that we had observed poor aseptic

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technique during the
(b) (4) of the product.

OBSERVATION 3

There is no written testing program designed to assess the stability characteristics of drug products.

Specifically,

A) Your firm has no documentation to justify the Beyond Use Date of injectable drug products up to 1000 days. From March 2012 to March 2013, your firm produced (b) lots of approximately 300 different sterile, injectable drug products with Beyond Use Dates (BUDs) up to 1000 days, to include preserved and preservative free drug product units which are not labeled as single-use. For example,

- HCG 5 K Lyophilized 5000 U Powder, lot #20130211@3, BUD 1000 days. In addition, the product BUD of 11/8/2015 exceeds the expiration date of the Sterile Water For Injection lot #23-508-FW, which has an expiration date of 11/1/2014.
- Magnesium Chloride 50 ml 200 mg/ml Inj., lot #20131010@15, BUD 636 days.

B) Your firm has not conducted anti-microbial effectiveness testing to determine whether (b) (4) (b) (4) effectively inhibit microbial growth in sterile injectable drug products through BUD. From March 2012 to March 2013, your firm produced (b) (4) lots of sterile injectable drug products containing these preservatives with BUD's up to 720 days. For example,

- Testosterone, 10ml, Preserved, 100mg/ml for Injection, lot #20120410@30 (Production date: 4/10/12 Beyond Use Date: 10/2/13) (BUD: 540 days) Contains: (b) (4)
- Pyridoxine, 30ml, Preserved, 100mg/ml for Injection, lot #20110808@12 (Production date: 8/8/11 Beyond Use Date: 7/28/13) (BUD: 720 days) Contains: (b) (4)
- Dextrose 50ml 50 for Injection (Production date: 9/28/12 Beyond Use Date: 3/27/13) (BUD: 180 days): Contains (b) (4)

C) Your firm has failed to conduct container integrity closure studies for any injectable drug products. Some examples consist of the following:

- Testosterone, 10ml, Preserved, 100mg/ml for Injection
- Pyridoxine, 30ml, Preserved, 10mg/ml for Injection
- Dextrose 50ml for Injection
- M.I.C. 30ml Preserved for Injection

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OBSERVATION 4

Procedures describing the handling of all written and oral complaints regarding a drug product are not followed.

Specifically, your SOP #9.008 entitled, "Complaint and Mishap Rectification" (Reviewed Date: 6/2/12) provides requirements for the evaluation of complaints. Review of return logs for the period between 3/2012 and 3/2013 revealed at least 20 instances where a quality-related complaint occurred but was not investigated. Some examples consist of the following:

1. Methylcobalamin Buffered, 30ml, 1mg/ml, lot #20120608@34 (Production date: 6/8/2012 Beyond Use Date: 6/8/2013)

Invoice#377054A dated 7/11/12 documented a customer complaint involving patients who had extreme pain at the injection site and were sent an older lot as a replacement.

2. Methylcobalamin Buffered, 30ml,1mg/ml, lot #20120904@7 (Production date: 9/4/12 Beyond Use Date: 8/1/13)

Invoice #383247A dated 9/11/12 documented a customer complaint involving pain and swelling at the injection site.

3. Methylcobalamin Buffered, 30ml, 1 mg/ml, lot #20120702@13 (Production date: 7/2/12 Beyond Use Date: 7/2/13)

Invoice #382353A dated 8/15/12 documented a customer complaint concerning painful injections from multiple patients.

4. Vitamin D3 50,000 IU/ml 5ml, lot #2012090@27

Invoice #383217A dated 11/2/12 documented a customer complaint concerning crystallization of the product.

5. L-Phenylalanine 50 ml, 10mg/ ml, lot #20120417@17

Invoice #35488A dated 6/27/12 documented a customer complaint concerning precipitation with the product.

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OBSERVATION 5

Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room and equipment to produce aseptic conditions.

Specifically,

A) Your firm has not conducted disinfectant effectiveness studies to demonstrate that disinfectants used in the ISO 5 and 7 areas can sufficiently reduce bioburden. Currently, your firm utilizes the following disinfectants:

- (b) (4)
- (b) (4)
- (b) (4)

B) The interior of the lyophilizer is not sterilized prior to use. Your firm wipes the the interior before use by using non-sterile wipes to apply (b) (4)

OBSERVATION 6

Equipment and utensils are not cleaned and maintained at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically, on 3/18/13, I (Investigator Stephen Brown) observed orange residue on the HEPA filters and filter manifolds installed on ISO 5 hood # 3 (one out of (b) flow hoods in the ISO 7 clean room). Some examples of drug product filled in Hood #3 and distributed during the week prior to 3/18/13 consist of the following:

- HCG 5 K Lyophilized 5000 U Powder, lot #20130314@23 (Production date: 3/14/2013 Beyond Use date: 12/1/14)
- Vitamin A Injection, lot #20130308@10 (Production date: 3/8/2013 Beyond Use Date: 9/4/2013)
- Cyanocobalamin, lot #20130313@19 (Production date: 3/13/2013 Beyond Use Date: 9/1/13)

No investigation was performed.

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OBSERVATION 7

Each batch of drug product required to be free of objectionable microorganisms is not tested through appropriate laboratory testing.

Specifically, your firm produced and distributed about (b) lots of injectable drug products for the period between 3/12-3/13. The sterility testing performed by your contract laboratory consists of a "Plate Contamination" test (b) (4)) or a (b) (4) test. However, your firm provided no data to demonstrate that either method is equivalent to or better than the USP 71 sterility method.

Sterility testing, as defined under USP 71, was conducted for only 2 lots during the designated time period.

In addition, testing for endotoxin was limited to about 200 lots.

Some examples of lots which were tested for "Plate Contamination" consist of the following:

- HCG 5 K Lyophilized 5000 U Powder, lot #20130211@3 (Production date: 2/11/2013 Beyond Use Date: 11/8/2015)
- Magnesium Chloride 50ml, 200mg/ml, lot #20130103@15 (Production date: 1/3/2013 Beyond Use Date: 10/1/14)
- Hyaluronic Acid, 10ml X-Link 20mg/ml, lot #20121101@20 (Production date: 11/1/2012 Beyond Use Date: 11/1/2013)

An example of a lot which was tested for (b) (4) was Methylcobalamin Buffered, 30ml, 1mg/ml for Injection, lot #20120904@7 (Production date: 9/4/12 Beyond Use Date: 8/1/13).

OBSERVATION 8

Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the identity and strength of each active ingredient prior to release.

SOP #8.011.2 entitled, "Potency Testing" (Date: 6/27/12) includes the following information:

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CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Dallas, TX 75244-5021	Producer of Sterile Drug Products

- All drug products made in multiple dose batches will undergo potency and sterility testing to ensure the proper strength of all components.
- Potency testing will be done all new formulations (first time formulations) of all sterile and non-sterile products to validate the drug formula and process.
- Product that is repeatedly produced may undergo Skip Batch Testing if repeatable results are obtained.
- All products must have a potency of between (b) (4) of the stated potency based on the formula.

Between 3/2012 and 3/2013, your firm produced and distributed about (b) lots of injectable drug products of which about 118 lots were tested for potency. Some examples of drug products which were not tested for potency include the following:

- Lipotonix Plus for Injection, lot #20111118@26 (Production Date: 11/18/2011 Beyond Use Date: 11/17/2012)
- HCG , 5 K Lyophilized 5,000 Units Powder, lot #20130211@3 (Production Date: 2/11/2013. Beyond Use Date: 11/8/2015)
- Magnesium Chloride 50ml 200mg/ml, lot #20130103@15 (Production date: 1/3/2013 Beyond Use

OBSERVATION 9

Protective apparel is not worn as necessary to protect drug products from contamination.

SOP #7.001 entitled, "Disposable Gowns, Masks, Gloves, Shoe Covers, etc." (Date: 6/21/12) includes the following requirements:

A. Gowns: "Appropriate gown should be chosen for type of compounding to be performed."
B. Masks: "Appropriate mask should be chosen for the type of compounding to be performed."
C. Footwear: "Appropriate shoe covers should be used and then disposed."

SOP #7.001 includes no requirements for the use of sterile gowns, masks, gloves, or shoe covers.

On 3/18/2013, we observed the sterile (b) (4) of the drug product, L-Carnitine 30ml 500mg/ml for Injection (lot #20130307@5). The technician used non-sterile gloves, mask, gown and (b) (4) in the ISO 5 work area.

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DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214) 253-5200 Fax:(214) 253-5314 Industry Information: www.fda.gov/oc/industry	03/18/2013 - 04/16/2013* FEI NUMBER 3000203232

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Mr. Raymond J. Bertrand, President and Pharmacist in Charge

FIRM NAME	STREET ADDRESS
Apothecure, Inc	4001 Mcewen Rd Ste 100
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OBSERVATION 10

Filled drug product containers which are set aside and held in an unlabeled condition are not identified to preclude mislabeling of individual containers, lots or portions of lots.

Specifically, on 3/18/13, multiple lots of unlabeled injectable drug products were observed in plastic totes contiguous with each other in the IV Room. The Formula Worksheet for each lot was observed attached to each tote. The different lots consist of the following:

1) Lipotocin Plus 10mL (Lot 20130307@8; Beyond Use Date 9/1/13): (b) (4) vials

2) MIC (Preserved) (Lot 20130301@19; Beyond Use Date 3/1/2014): (b) (4) vials

3) Procaine (buffered) 2% 30mL (Lot 20130305@1; Beyond Use Date 9/5/13): (b) (4) vials

4) MSM 200mg/ml 30 mL (Lot 20130228@9; Beyond Use Date 8/28/2013): (b) (4) vials

5) Tranquil Inj. 10mL (Lot 20130266@6; Beyond Use Date 8/26/2013) (b) (4) vials

6) Glycyrrhizic Acid 8mg/ml (Lot 20130227@7; Beyond Use Date 2/27/2014): (b) (4) vials

7) Cyanocablamin Buffered 1mg/ml (Lot 20130313@19; Beyond Use Date 3/13/14) (b) (4) vials

8) Cyanocabalamin Buffered 1mg/mL (Lot 20130313@14; Beyond Use Date 9/13/2013): (b) (4) vials

9) MIC Preserved 50mL, (Lot 2013031@3; Beyond Use Date 10/31/13): (b) (4) vials

10) Phosphatidylcholine/ Deoxycholic Acid IV (Lot 20130308@13; Beyond Use Date 12/31/13): (b) (4) vials

11) Prototherapy #1 Stock Solution 10mL,(Lot 20130227@17; Beyond Use Date 8/26/13): (b) (4) vials

OBSERVATION 11

Master production and control records lack complete manufacturing and control instructions and specifications.

Specifically, your firm does not consistently document the name/lot number of the (b) (4) used in the sterilization

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of injectable drug products. For example, M.I.C. 50ml Preserved for Injection, lot #20121213@9.

OBSERVATION 12

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically,

A. SOP #9.043 entitled, "Measuring Particulate Matter Levels within the Compounding Hoods" (Date: 6/2012) provides guidance for the frequency and type of testing related to monitoring for particulates. For example,

- Testing for viable air monitoring is conducted every (b) (4) in each ISO 5 hood under static conditions. The most recent testing for viable air monitoring was on 1/4/2013.
- Testing for non-viable particulate testing is conducted every (b) (4) in the ISO 5 hoods under static conditions. The most recent testing for non-viable air monitoring was on 1/4/2013.

B. SOP #9.038 entitled, "Surface Sampling Plan" (Date: 1/2012) provides guidance for the sampling of cleanroom surfaces and operator's gloves. The SOP indicates that monitoring of surfaces and fingertips of gloves should be conducted every (b) (4) Review of your firm's monitoring data for surface and gloves revealed that documentation was not available for monitoring for surface and personnel for the following months:

- Surface: No data
- Personnel (Gloved sampling): Testing was conducted in 10/12 only.

C. In addition, SOP #5.004 entitled, "Media Paddle Testing (Enviro Test) for the Sterile IV Room" (Date: 11/8/12) provides requirements for the surface monitoring of the ISO 5 and 7 areas monthly using media paddles. Review of monitoring data revealed that testing was not conducted for the following months:

- March 2012-October 2012
- February 2013-March 2013

D. Your firm has not established a specification for pressure differentials between the ISO 5 and ISO 7 areas.

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E. The interior of the lyophilizer is not monitored for viable contaminants before and after use.

OBSERVATION 13

There are no written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess.

Specifically, your firm utilizes a (b) (4) for the lyophilization of injectable drug products. Your firm has failed to validate the different cycles used for the lyophilization of the drug products, Human Chorionic Gonadotropin Lyophilized 5,000 Units Powder and Sermorelin. Some examples of specific cycle parameters consist of the following:

Freezing	Duration	HCG (Human Chorionic Gonadotropin)	Sermorelin
(b) (4)	[redacted]	[redacted]	[redacted]
Primary [redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]

Prior to lyophilization, drug product is sterile (b) (4) in an ISO 5 hood and aseptically transferred to individual vials which are then partially stoppered in the ISO 5 hood. The vials are then carried on a tray through an ISO 7 area and placed inside the lyophilizer through a door which is open to the ISO 7 environment.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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*** DATES OF INSPECTION:**
03/18/2013(Mon), 03/19/2013(Tue), 03/20/2013(Wed), 03/21/2013(Thu), 03/22/2013(Fri), 03/25/2013(Mon), 03/26/2013(Tue), 03/27/2013(Wed), 03/28/2013(Thu), 03/29/2013(Fri), 04/04/2013(Thu), 04/05/2013(Fri), 04/08/2013(Mon), 04/09/2013(Tue), 04/10/2013(Wed), 04/11/2013(Thu), 04/12/2013(Fri), 04/15/2013(Mon), 04/16/2013(Tue)

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